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EXAMINER	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/687,479	RISER ET AL.	
	Examiner	Art Unit	
	Nora M. Rooney	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,7-10,13-16,19-23,26-29,32-35 and 37-47* is/are pending in the application.

4a) Of the above claim(s) *13-16,19,40,41,45,46,50 and 51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 7-10, 20-23, 26-29, 32-35, 37-39, 42-44, 47-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/15/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-4, 7-10, 13-26, 19-23, 26-29, 32-25 and 37-47 are pending.

2. Applicant's election with traverse of Group I, now claims 1-4, 7-10, 20-23, 26-29, 32-35, 37-39, 42-44 and 47-49 and the species of hyperglycemia in the reply filed on 03/08/2007 is acknowledged. The traversal is on the grounds that the methods for diagnosing a renal disorder do not require different ingredients, method steps, and endpoints from the methods of identifying a predisposition or susceptibility to a renal disorder. Applicant also argues that the disease species of hyperglycemia, glomerular mechanical strain, hypertension, diabetes, diabetic neuropathy, glomerusclerosis and glomerulonephritis recited in the claims because the etiologies are typified by a common feature and because the desired therapeutic effect of all the disease is a decreased level of CTGF expression.

This is not found persuasive for many reasons. First, the ingredient that differs between the method of diagnosing and the method predicting a renal disorder is the patient sample. The patient sample from one with renal disease will be qualitatively different from a patient sample from one who does not yet have renal disease. Further, the diseases of hyperglycemia, glomerular mechanical strain, hypertension, diabetes, diabetic neuropathy, glomerusclerosis and glomerulonephritis are not the same, nor is there one etiology or therapeutic effect for the disorders. The etiologies and therapeutic effects are inherent features of the diseases that are not determined by applicant to fit the purposes of their invention. Applicant's general assertion that the methods are the same is without merit because a method of diagnosing a renal disease that is

already present is very different from a method of predicting the onset of renal disease. If CTGF causes disease, then the disease is there and it is a method of diagnosis. If CTGF is a marker that is frequently associated with disease, then it is not a method of diagnosis. So, an increased level of CTGF in the patient sample either diagnoses or predicts renal disease, but not both.

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 13-16, 19, 40-41, 45-46 and 50-51 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 03/08/2007.

4. Claims 1-4, 7-10, 20-23, 26-29, 32-35, 37-39, 42-44 and 47-49 are currently under examination as they read on a method for diagnosing a renal disorder.

5. Applicant's IDS document filed on 12/15/2003 is acknowledged.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 1-4, 7-10, 20-23, 26-29, 32-35, 37-39, 42-44 and 47-49 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The minimum

requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized, and a correlation step describing how the results of the assay allow for the determination. In claims 1, 7, 20, 26 32, 37, 42 and 47 and Claims dependent thereupon, it is unclear how CTGF is detected in the subject sample to determine the level of CTGF. While all of the technical details of a method need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The minimum requirements for method steps minimally include a contacting step in which the reaction of the sample with the reagents necessary for the assay is recited, a detection step in which the reaction steps are quantified or visualized and a correlation step describing how the results of the assay allow for the determination. Claims 1, 7, 20, 26 32, 37, 42 and 47 and Claims dependent thereupon are missing a contact step that would give an indication of how CTGF is detected in the subject sample.

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 1-4, 7-10, 20-23, 26-29, 32-35, 37-39, 42-44 and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is not enabled for: a method for **diagnosing a renal disorder associated with increased glucose** in a subject, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 1; wherein the increased glucose is associated with diabetes of claim 2; wherein the sample is a urine sample of claim 3; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 4; A method for **diagnosing a renal disorder in a subject having hyperglycemia**, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 7; wherein the hyperglycemia is associated with diabetes of claim 8; wherein the sample is a urine sample of claim 9; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 10; A method for **diagnosing a renal disorder associated with glomerular mechanical strain in a subject**, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 20; wherein the glomerular mechanical strain is associated with diabetes of claim 21; wherein the sample is a urine sample of claim 22; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 23; A method for **diagnosing a renal**

disorder in a subject having hypertension, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 26; wherein the hypertension is associated with diabetes of claim 27; wherein the sample is a urine sample of claim 28; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 29; A method for **diagnosing a renal disorder in a subject having diabetes**, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 32; wherein the sample is a urine sample of claim 33; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 34; **wherein the renal disorder is diabetic nephropathy** of claim 35; A method for **diagnosing diabetic nephropathy in a subject**, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 37; wherein the sample is a urine sample of claim 38; detecting the level of CTGF comprises using a CTGF-specific antibody of claim 39; A method for **diagnosing glomerulosclerosis in a subject**, the method comprising: (a) obtaining a urine sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of glomerulosclerosis of claim

42; wherein the glomerulosclerosis is associated with diabetes of claim 43; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 44; A method for **diagnosing glomerulonephritis in a subject**, the method comprising: (a) obtaining a urine sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of glomerulonephritis of claim 47; wherein the glomerulonephritis is associated with diabetes of claim 48; wherein detecting the level of CTGF comprises using a CTGF- specific antibody of claim 49.

The specification disclosure does not enable one skilled in the art to practice the invention without an undue amount of experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the lack of sufficient working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Pages 46-57 of the specification disclose in vitro mouse data showing a correlation between the presence of CTGF in various kidney samples and cells with renal disease. Page 57 discloses the detection of CTGF in urine from 8 "patients being treated with a variety of kidney

diseases" and from 3 normal healthy controls. Applications 60/099,471 and 60/112,855 disclose that 4 of the 8 patients were diabetic, but the instant application discloses that 3 of the 8 patients were diabetic (Examiner requests clarification). In any case, it was found that all 8 patient samples (100%) and 1 normal healthy control sample (33%) had detectable CTGF. A small CTGF fragment was present in 3 out of 4 diabetic patients according to 60/099,471 and 60/112,855 and 3 out of 3 diabetic patients according to the instant specification.

The specification does not disclose a method of detecting CTGF in a patient sample that diagnoses diabetic neuropathy, glomerulosclerosis, glomerulonephritis, or a renal disorder associated with increased glucose, in a subject having hyperglycemia, associated with glomerular mechanical strain or in a subject having hypertension. At the very best, Example 12 discloses a method of detecting a renal disorder in a subject having diabetes by detecting CTGF in urine. However, 1 out of the 3 control patients also had CTGF in their urine, which shows that the ability to diagnose any renal disease on the basis of the level of CTGF is very unpredictable. Nguyen et al. teaches that although the mean urinary CTGF level of patients with diabetic neuropathy was 1.6 fold higher than in control subjects that there was extensive overlap between patient and control groups. So, although it is statistically significant, the difference is less impressive in this large-scale study than was previously reported (PTO-892, Reference U, page 86, middle column, second full paragraph). It is suggested that the level of CTGF among patient samples correlates with severity of renal disease, rather than presence since control levels overlapped with patient samples (In particular, page 87, last paragraph). The reference goes on to teach that clinical studies will be necessary to evaluate urinary CTGF as an additional

parameter for monitoring renal function in diabetic neuropathy (In particular, page 87, last paragraph). Therefore, the art shows that using CTGF to diagnose any single renal disease is unpredictable, much less all of the recited renal diseases and pathologies.

The recited 'sample' from a patient encompasses any fluid or tissue sample, including many samples that would not work such as hair and bone. Example 12 in the specification on page 57 discloses the use of urine to detect CTGF for diagnosing the various renal disorders. There is no guidance in the specification nor any example of any other patient sample that can be used in the instant invention other than urine. Nguyen et al. teaches that it is unclear how much plasma CTGF levels contribute to urinary CTGF levels, as CTGF is predicted to be cleared from plasma by glomerular filtration. Local production of CTGF in the kidney and renal filtration of plasma could both contribute to CTGF levels in urine. More studies are needed to determine the role of plasma CTGF levels and renal disease. Because of the unpredictability of CTGF levels in other patient samples, it would require undue experimentation by one of ordinary skill in the art to practice the claimed invention commensurate in scope with the claims.

Reasonable correlation must exist between the scope of the claims and scope of the enablement set forth. In view on the quantity of experimentation necessary the limited working examples, the nature of the invention, the state of the prior art, the unpredictability of the art and the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

10. Claims 1-4, 7-10, 20-23, 26-29, 32-35, 37-39, 42-44 and 47-49 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of: a method of diagnosing a renal disorder in a subject having diabetes comprising obtaining a urine sample from the subject, contacting the urine sample with an antibody specific for CTGF, detecting the level of CTGF protein in the sample and comparing the level of CTGF in the sample to a standard level of the CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of a renal disorder.

Applicant is not in possession a method for diagnosing a renal disorder associated with increased glucose in a subject, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 1; wherein the increased glucose is associated with diabetes of claim 2; wherein the sample is a urine sample of claim 3; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 4; A method for diagnosing a renal disorder in a subject having hyperglycemia, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of

claim 7; wherein the hyperglycemia is associated with diabetes of claim 8; wherein the sample is a urine sample of claim 9; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 10; A method for diagnosing a renal disorder associated with glomerular mechanical strain in a subject, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 20; wherein the glomerular mechanical strain is associated with diabetes of claim 21; wherein the sample is a urine sample of claim 22; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 23; A method for diagnosing a renal disorder in a subject having hypertension, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 26; wherein the hypertension is associated with diabetes of claim 27; wherein the sample is a urine sample of claim 28; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 29; A method for diagnosing a renal disorder in a subject having diabetes, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 32; wherein the sample is a urine sample of claim 33; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 34; wherein the renal disorder is diabetic nephropathy of claim 35; A method

for diagnosing diabetic nephropathy in a subject, the method comprising: (a) obtaining **a sample** from the subject; (b) detecting the level of CTGF protein in **the sample**; and (c) comparing the level of CTGF protein in **the sample** to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder of claim 37; wherein the sample is a urine sample of claim 38; detecting the level of CTGF comprises using a CTGF-specific antibody of claim 39; A method for diagnosing glomerulosclerosis in a subject, the method comprising: (a) obtaining a urine sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of glomerulosclerosis of claim 42; wherein the glomerulosclerosis is associated with diabetes of claim 43; wherein detecting the level of CTGF comprises using a CTGF-specific antibody of claim 44; A method for diagnosing glomerulonephritis in a subject, the method comprising: (a) obtaining a urine sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of glomerulonephritis of claim 47; wherein the glomerulonephritis is associated with diabetes of claim 48; wherein detecting the level of CTGF comprises using a CTGF- specific antibody of claim 49.

Applicant has disclosed a method of diagnosing a renal disorder by detecting the level of CTGF protein in a urine sample. The 'sample' genus recited in the claims encompasses many

samples that were not described in the specification to such a degree that one of ordinary skill in the art would know what samples can be used in the instant invention other than a urine sample.

Adequate written description requires more than a mere statement that it is part of the invention. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC1993). The Guidelines for the Examination of Patent Application Under the 35 U.S.C.112, ¶ 1"Written Description" Requirement make clear that the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species disclosure of relevant, identifying characteristics, i.e., structure or other physical and or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the genus (Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 20001, see especially page 1106 3rd column).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath

at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the final Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

Claim Rejections - 35 USC § 102

11. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

12. Claims 1-2, 4, 7-8, 10, 20-21, 23, 26-27, 29, 32, 34-35, 37 and 39 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,232,064 (PTO-892, Reference A) as

evidenced by the specification on page 2 paragraphs [0007] and [0008]; and page 4, paragraph [0012].

The '064 patent teaches a method for diagnosing a renal disorder associated with increased glucose (kidney fibrosis) in a subject, the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder; wherein the increased glucose is associated with diabetes; wherein detecting the level of CTGF comprises using a CTGF-specific antibody; A method for diagnosing a renal disorder in a subject having hyperglycemia (kidney fibrosis), the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder (kidney fibrosis); wherein the hyperglycemia is associated with diabetes; wherein detecting the level of CTGF comprises using a CTGF-specific antibody; A method for diagnosing a renal disorder associated with glomerular mechanical strain (kidney fibrosis) in a subject, the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder; wherein the glomerular mechanical strain is associated with diabetes; wherein detecting the level of CTGF comprises using a CTGF-specific antibody; A method for diagnosing a renal disorder in a subject having

hypertension (kidney fibrosis), the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder; wherein the hypertension is associated with diabetes; wherein detecting the level of CTGF comprises using a CTGF-specific antibody; A method for diagnosing a renal disorder in a subject having diabetes (kidney fibrosis), the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder; wherein detecting the level of CTGF comprises using a CTGF-specific antibody; wherein the renal disorder is diabetic nephropathy; A method for diagnosing diabetic nephropathy (kidney fibrosis) in a subject, the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein in the sample; and (c) comparing the level of CTGF protein in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein is indicative of the presence of the renal disorder; wherein the sample is a urine sample; and detecting the level of CTGF comprises using a CTGF-specific antibody (In particular, claims 1-2, column 2, lines 57-63, column 5, lines 13-26, column 10, line 51 to column 11, line 14).

The specification on page 2 paragraphs [0007] and [0008]; and page 4, paragraph [0012] teaches that diabetic neuropathy, glomerulosclerosis, glomerulonephritis, and renal disorders associated with increased glucose, in a subject having hyperglycemia, associated with glomerular

mechanical strain or in a subject having hypertension are all have kidney fibrosis as a common pathway to progression.

The reference teachings anticipate the claimed invention.

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claims 3, 9, 22, 28, 33, 38 42-44 and 47-49 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 6,232,064 (PTO-892, Reference A) in view of U.S. Patent 5,753,517 (PTO-892, Reference B) as evidenced by the specification on page 2 paragraphs [0007] and [0008]; and page 4, paragraph [0012].

The '064 patent has been discussed *supra*.

The claimed invention differs from the prior art by the recitation of wherein the sample is urine.

The '517 patent teaches using urine to detect the level of urinary albumin to assess renal function and degree of kidney damage (In particular, column 1, lines 16-19, column 3, lines 6-11, column 9, lines 47-55 and claims 1 and 9).

It would have been obvious to use the urine sample of the '517' patent in the method of diagnosing a renal disorder associated with kidney fibrosis of the '064 patent because the '064 patent teaches using a sample suspected of containing CTGF. The '517 patent teaches that urine is a sample containing a marker (albumin) that is associated with kidney damage and renal dysfunction. Therefore, it would have been obvious to one of ordinary skill in the art to use a sample that comes directly from kidneys which has been known in the past to contain markers for kidney damage and renal dysfunction in the method for diagnosing a renal disorder by measuring the level of CTGF in that sample.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

15. Claims 1-2, 7-8, 20-21, 26-27, 32, 35 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Ito et al. (IDS filed on 12/15/2003) in view of Gygi et al. (PTO-892, Reference V).

Ito et al. teaches a method for diagnosing a renal disorder associated with increased glucose in a subject (diabetic nephropathy), the method comprising: (a) obtaining a sample (kidney specimen) from the subject; (b) detecting the level of CTGF protein (mRNA) in the sample; and (c) comparing the level of CTGF protein (mRNA) in the sample to a standard level of CTGF protein, wherein an increased level of CTGF protein (mRNA) is indicative of the presence of the renal disorder; wherein the increased glucose is associated with diabetes (diabetic nephropathy); A method for diagnosing a renal disorder in a subject having hyperglycemia (diabetic nephropathy), the method comprising: (a) obtaining a sample (kidney specimen) from the subject; (b) detecting the level of CTGF protein (mRNA) in the sample; and (c) comparing the level of CTGF protein (mRNA) in the sample to a standard level of CTGF protein (mRNA), wherein an increased level of CTGF protein (mRNA)is indicative of the presence of the renal disorder; wherein the hyperglycemia is associated with diabetes (diabetic nephropathy); A method for diagnosing a renal disorder associated with glomerular mechanical strain (diabetic nephropathy) in a subject, the method comprising: (a) obtaining a sample (kidney specimen) from the subject; (b) detecting the level of CTGF protein (mRNA) in the sample; and (c) comparing the level of CTGF protein (mRNA) in the sample to a standard level of CTGF protein(mRNA), wherein an increased level of CTGF protein (mRNA) is indicative of the presence of the renal disorder; wherein the glomerular mechanical strain is associated with

diabetes (diabetic nephropathy); A method for diagnosing a renal disorder in a subject having hypertension (diabetic nephropathy), the method comprising: (a) obtaining a sample (kidney specimen) from the subject; (b) detecting the level of CTGF protein (mRNA) in the sample; and (c) comparing the level of CTGF protein (mRNA) in the sample to a standard level of CTGF protein (mRNA), wherein an increased level of CTGF protein (mRNA) is indicative of the presence of the renal disorder; wherein the hypertension is associated with diabetes (diabetic nephropathy); A method for diagnosing a renal disorder in a subject having diabetes (diabetic nephropathy), the method comprising: (a) obtaining a sample (kidney specimen) from the subject; (b) detecting the level of CTGF protein (mRNA) in the sample; and (c) comparing the level of CTGF protein (mRNA) in the sample to a standard level of CTGF protein (mRNA), wherein an increased level of CTGF protein (mRNA) is indicative of the presence of the renal disorder; wherein the renal disorder is diabetic nephropathy; A method for diagnosing diabetic nephropathy in a subject, the method comprising: (a) obtaining a sample from the subject; (b) detecting the level of CTGF protein (mRNA) in the sample; and (c) comparing the level of CTGF protein (mRNA) in the sample to a standard level of CTGF protein (mRNA) and wherein an increased level of CTGF protein (mRNA) is indicative of the presence of the renal disorder (In particular, Table 1, paragraph spanning pages 853 and 854, paragraph spanning pages 854 and 855; 'Results', whole document).

Claims 1-2, 7-8, 20-21, 26-27, 32, 35 and 37 are included in this rejection because CTGF mRNA expression is an indirect measure of CTGF protein.

The claimed invention differs from the prior art by the recitation of measuring CTGF protein instead of mRNA.

Gygi et al. teaches that the correlation between mRNA and protein levels is insufficient to predict protein expression levels from quantitative mRNA data.

One of ordinary skill in the art would have been motivated to measure protein as taught by Gygi et al. in the CTGF detection method of Ito et al. because Gygi teaches that mRNA expression levels are not a good indication of CTGF protein expression levels. Therefore, it would be obvious to measure the CTGF protein levels in the renal fibrosis kidney specimens to confirm the mRNA results.

From the reference teachings, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the reference, especially in the absence of evidence to the contrary.

16. No claim is allowed.

17. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nora M. Rooney whose telephone number is (571) 272-9937. The examiner can normally be reached Monday through Friday from 8:30 am to 5:00 pm. A

message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 9, 2007

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